RELIABILITY OF K-TIRADS IN EVALUATION OF THYROID NODULES: COMPARISON WITH FNAC IN PATIENTS REFERRED FOR THYROID ULTRASOUND AT MUHIMBILI TERTIARY HOSPITALS.

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By

Seleman Fadhili

A Dissertation Submitted in (Partial) Fulfillment of the Requirement for the Degree of Master of Medicine (Radiology) of

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CERTIFICATION

The undersigned certifies that he has read and hereby recommend for acceptance of dissertation entitled "**Reliability of K-TIRADS in evaluation of thyroid nodules: Comparison with FNAC in patients referred for thyroid ultrasound at Muhimbili Tertiary Hospitals**" in fulfillment of the requirement for the degree of Master of Medicine (Radiology) of Muhimbili University of Health and Allied Sciences.

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Prof Ahmed Jusabani

(Supervisor)

Date: ________________________

DECLARATION AND COPYRIGHT

I, **Seleman Fadhili,** declare that this dissertation entitled **"Reliability of K-TIRADS in evaluation of thyroid nodules: Comparison with FNAC in patients referred for thyroid ultrasound at Muhimbili Tertiary Hospitals."** is my own original work and that it has not been presented and will not be presented to any other university for similar or any other degree award.

Signature___________________________ Date___________________________________

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ABSTRACT

Background: Thyroid nodules are relatively common worldwide with a malignancy potential in 5%. Studies show prevalence of nodules in up to 68% of the population using Ultrasound (USS). Recent studies have revealed that USS features can be used to screen for thyroid malignancy without necessity for biopsy in every thyroid nodule. Korean Thyroid Imaging Reporting and Data System (K-TIRADS) is among the modified sonographic risk stratification system for thyroid nodules which makes use of greyscale USS findings regardless of clinical information. We assessed the reliability of K-TIRADS in predicting the nature thyroid nodules using Fine Needle Aspiration Cytology (FNAC) as Gold standard in patients referred for thyroid USS at Muhimbili National Hospital (MNH) and MUHAS Academic Medical Center (MAMC) from October 2018 to April 2019.

Objective: To determine the reliability the Korean Thyroid Imaging Reporting and Data System (K-TIRADS) in evaluation of thyroid nodules in patients referred for thyroid ultrasound at Muhimbili Tertiary hospitals from October 2018 to April 2019.

Methodology: This was a cross sectional hospital based study which involved 96 Patients with thyroid nodules referred to Imaging Department for thyroid Ultrasound at MNH and MAMC.

Data collection was done using a structured questionnaire filled by the principal investigator.

Thyroid ultrasound was performed and imaging findings reported by the Principal Investigator, confirmed by a radiologist. In case of disagreement a second radiologist was consulted and the conclusion was reached by consensus. K-TIRADS categories for each nodule were then determined. FNAC was done by pathologist for palpable nodules. For non-palpable nodules the Principal Investigator and pathologist collaborated under USS guidance to take the samples. Smears for FNAC were prepared and interpreted by the Pathologist. Ultrasound findings were compared with cytology results as the “Gold standard”. Statistical Package for Social Sciences (SPSS) version 23 was used for data analysis. Sensitivity, Specificity, Positive and Negative predictive values and malignancy risk of K-TIRADS were determined. X^2 test was used for inferential statistics of categorical variables. Spearman’s rank correlation test was used to assess the relationship between categories of K-TIRADS and

Cytology results. A p value of less than 0.05 was considered significant at 95% confidence level.

Results: Majority of participants were females with Male to female ratio 1:8**.** The age range was from 6 to 92 years .The rate of malignancy was higher in the >40 age group. The risk of malignancy for K-TIRADS 2, 3, 4 and 5 were 0%, 3.8%, 44.1% and 100% respectively. Using K-TIRADS 3(for nodules ≥1.5cm) , K-TIRADS 4 and K-TIRADS 5 as criteria for malignancy the Sensitivity, Specificity, Positive Predictive Value(PPV) and Negative Predictive Value (NPV) a were 100%, 42.7%, 12.1% and 100% respectively.

Conclusion: Females constitute the majority of thyroid nodule patients.

Age above 40 years is a risk for thyroid malignancy.

Majority of thyroid nodules are in K-TIRADS 3 category.

Malignancy risk increases with the order of K-TIRADS category.

K-TIRADS criteria demonstrates a very high sensitivity for thyroid malignancy and therefore a reliable screening tool.

Recommendation: Patients with thyroid nodules can undergo ultrasound assessment using K-TIRADS as the first modality. Patients diagnosed with benign thyroid nodules using K-TIRADS may not need further invasive screening (e.g FNAC).

A community based study with a large sample is suggested to obtain more evidence for implementation of K-TIRADS.

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LIST OF ABBREVIATIONS

BIRADS	Breast Imaging Reporting and Data System
CT	Computed Tomography
FDG	Fluorodeoxyglucose
FNAC	Fine Needle Aspiration Cytology
K-TIRADS	Korean Thyroid Imaging Reporting and Data System
MAMC	MUHAS Academic Medical Centre
MUHAS	Muhimbili University of Health and Allied Sciences
MNH	Muhimbili National Hospital
MRI	Magnetic Resonance Imaging.
NPV	Negative Predictive Value
PET	Positron Emission Tomography
PPV	Positive Predictive Value
TIRADS	Thyroid Imaging Reporting and Data System
USS	Ultrasonography /Ultrasound

DEFINITION OF TERMS

i. **Echogenicity:** Brightness of the dots generated by returning echoes from the body.

ii. **Echotexture**: Refers to the uniformity of echoes within a structure

iii**. Microcalcification**: Echogenic foci of 1 mm or less with or without posterior acoustic shadowing within solid portion of a mass

iv.**Muhimbili Tertiary Hospitals**: Muhimbili National Hospital and MUHAS Academic Medical Centre (MAMC)

v. **Reliability:** Refers to whether or not you get the same findings by using an instrument to measure something more than once.

vi. **Sonography**: Imaging of a structure using ultrasound

vii.**Solidity**: The solid and/ or cystic nature of internal contents in a nodule.

viii. **Sensitivity:** Ability of a test to give positive findings amongst those truly diseased in a given study (Measure of a true positive)

ix. **Specificity:** Ability of a test to give negative findings amongst those not diseased in given study (Measure of true negative).

x. **Positive predictive value**: Proportion of the diseased amongst all those who tested positive.

xi.**Negative predictive value**: Proportion of the not diseased individuals amongst all those who tested negative.

CHAPTER ONE

1.0. INTRODUCTION

1.1 Background

1.11 Normal anatomy of the thyroid

The thyroid is a bilobed butterfly shaped endocrine gland in the anterior neck. It rests on the trachea with its isthmus below the cricoid cartilage. In about half of the population a third lobe (pyramidal lobe) is present. The gland is related to the strap muscles anteriorly and sternocleidomastoid muscles anterolaterally. Posterior to the main lobes are the longus coli muscles. The lateral landmark of each lobe are the common carotid arteries. The transverse and anteroposterior diameters of any of the main thyroid lobes measure less than 2cm .The longitudinal lengths of either lobe is 4-6cm while the isthmus measures about 4mm in thickness.The isthmus is immediately anterior to the trachea and the esophagus lies posterior to the trachea (1).

Fig 1: Graphic image of Normal thyroid showing its two lobes joined at isthmus (Courtesy of Netter F. Atlas of Human Anatomy)

1.12 Ultrasound (USS) appearance

On ultrasound a normal thyroid is homogenous in echotexture and hyperechoic to the adjacent muscles. The capsule may appear as a thin hyperechoic line. Thyroid enlargement can be due to a diffuse disease or nodule(s). Thyroid nodules may be benign or malignant.

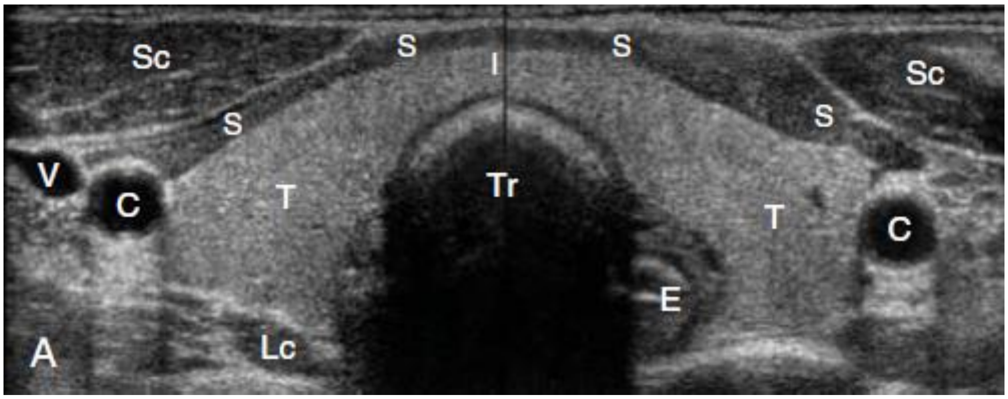


Fig 2.Normal thyroid appearance on ultrasound, Sc-Sternocleidomastoid muscle, S-Strap muscles, V-Internal jugular vein, C-Common carotid artery, T-Thyroid lobes, ,Lc-Longus coli muscles, E-Esophagus, Tr-Trachea(1).

1.13 Bethesda System for reporting thyroid Fine Needle Aspiration Cytology (FNAC)

The Bethesda system developed by the American Society for Clinical Pathology is commonly used to standardize cytology reporting among pathologists and aids a common understanding of all practitioners in the workup of thyroid nodules. It classifies cytology findings of nodules into six categories, ranging from category II denoting benign to category V denoting suspicious for malignancy and category VI implying malignant. Category I means non-diagnostic or unsatisfactory sample. It further indicates the risk of malignancy suggested by the categories ranging from 0-4% in category I and II with the risk of 97-99% in category VI. Respective management recommendations are also put forward (2).

Thyroid diseases are common in the African continent and worldwide. Thyroid carcinoma is relatively common worldwide, papillary and follicular cancers being the commonest histologic subtypes (3,4).

There is shortage of diagnostic services for thyroid nodules in most parts of Africa. USS and USS guided FNAC are the frequently used investigation methods. In few centers nuclear studies are also employed. The relatively expensive modalities like Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are also available in some facilities. Notwithstanding, their utilization is limited by higher examination fees with health care financing systems which are often cash based (5).

Studies have shown significant accuracy of ultrasound features of thyroid nodules when compared to cytology. We can therefore use ultrasound features to decide which nodules need to undergo further workup. (6).

1.2. Literature review

1.2.1 Socio-Demographic factors

Thyroid nodules are still important worldwide, carrying malignant potential of 5% (7,8). Women are affected more than men with a Male to Female ratio of 1:7-13 (12). With regard to thyroid malignancy papillary carcinoma is the commonest occurring histological subtype. The rest are relatively less common constituting about 22%. Anaplastic thyroid cancer characteristically occurs in old age with a poor prognosis (9–11). Family history of thyroid malignancy is a recognized risk for both differentiated thyroid carcinoma and medullary thyroid carcinoma. Both types generally have the best prognosis. Multiple Endocrine Neoplasia is a syndrome comprising of Familial Medullary thyroid carcinoma and other tumors of endocrine origin (9). Many studies show that thyroid nodules are prevalent in 2–6% of the population by physical examination, up to 68% using USS and from 8-65% in autopsy studies (10,13,14). Reported prevalence of endemic goiter in Africa ranges from 1%-90% depending on a country. In Tanzania endemic goiter is estimated to be 6.9% in people aged 6-12 years (5,15). Appropriate management of thyroid nodules lies in the ability to investigate the patient and precisely differentiate between benign and malignant nodules. Generally speaking, most parts of Africa are resource poor and diagnostic facilities are scarce. Consequently, the level diagnostic workup and management of thyroid disorders in the continent is still very low (5).

1.2.2 Risk factors for thyroid nodule(s)

Previous exposure to radiation especially in childhood is a well-documented risk factor for thyroid cancer worldwide (9,16). In Africa iodine deficiency appears to be the most important risk factor for thyroid malignancy. This has necessitated mass iodization campaigns as a preventive measure (5). A recent study done in Tanzania shows that a prolonged iodine deficiency state is associated with increased risk of developing malignant thyroid nodule(s). It points out that as many as 75% of patients with thyroid cancer are coming from low-iodine regions (17).

Goitrogenic substances such as cyanates found in cassava and selenium insufficiency have also been implicated (5).

1.2.3 Imaging modalities for Thyroid gland

Current first line modalities of thyroid investigations include Ultrasound and ultrasound guided FNAC. USS is a commonly used first modality due to the fact that it is non-invasive, relatively cheap, radiation free and easily operated. Its main drawback is being highly user dependent, such that different users may differ in their interpretation of a given nodule (18).

Computed tomography (CT) is a 3D imaging modality and is especially useful in nodules with calcifications, extra capsular extension and in identifying metastases. In most cases CT performed for other neck lesions may show thyroid lesions as incidental findings. However, CT has a disadvantage of using ionizing radiation. Furthermore, the use of iodinated contrast in CT interferes with iodine uptake of the thyroid making it impossible for the patient to perform iodine based nuclear studies or treatment for up to 6 months post CT imaging. The cost of CT imaging is also relatively high.

Positron emission Tomography (PET) and PET-CT scan can localize primary tumor and detect distant metastasis but have decreased sensitivity for differentiated thyroid cancer. Nonetheless, as the tumor turns undifferentiated the avidity to FDG uptake and thus the sensitivity of PET-CT increases.

Magnetic Resonance Imaging (MRI) is another 3D imaging modality which has the advantage of not using radiation. It has the best soft tissue contrast resolution and can be used to search for local invasion and metastases. Despite this capability it cannot be used to identify histological types of thyroid nodules and has the disadvantage of not allowed for people with metal implants and people with claustrophobia. It is also expensive compared to other modalities (9).

Radionuclide Scintigraphy can provide imaging as well as functional information about thyroid nodule(s). A hyper functioning nodule shows increased uptake of the radiopharmaceutical. It is also possible to evaluate for metastasis using full body radioiodine scans. Its disadvantages are radiation exposure, poor resolution of images, allergy to radiopharmaceuticals and reduced specificity as a cold nodule can be benign or malignant. The utilization of diagnostic nuclear imaging is still very low in the continent (5).

In practice the ultimate management of thyroid nodules lies on mutual conclusion of thyroid hormonal assay, USS and FNAC results (18).

1.2.4 TIRADS Ultrasound features

Several studies have attempted to characterize thyroid nodules based on the risk of malignancy. Features like shape, Contents, Margins, Echogenicity, Size, echogenic foci and color flow Doppler characteristics have been studied. Working with these ultrasound features is puzzling because of their variation (19). It has been difficult to develop a widely acceptable, adoptable and adaptable ultrasound classification system to differentiate benign from malignant nodules. Nevertheless, it is known that some Sonographic appearances are more often seen in malignant than in benign nodules (20). Some of the studies have evaluated these features individually but this has proved to be ineffective. Given this challenge, some have gone further to study both sole and combined ultrasound features and ultimately the value of using combination of features has been revealed (18,21–23). One study suggests combining both USS features and cytology findings to make a conclusion of malignancy. It advocates that a lesion is highly likely malignant when both ultrasound and cytology used together for the same lesion show suspicious results for malignancy. Moreover, it proposes that a lesion suspicious features on ultrasound and negative findings on cytology should have FNAC repeated (6). It is therefore clear that there have been variable attempts to categorize thyroid nodules in relation to risk of malignancy.

In 2009 Horvath et al (24) proposed a system called TIRADS (Thyroid Imaging Reporting and Data System), closely related to the Breast Imaging Reporting and Data System (BI-RADS) used in breast imaging (25). The USS features studied are echotexture, shape, echogenicity, orientation, acoustic transmission, surface, presence or absence of a capsule, borders, calcifications, and vascularity. The main goal was to have cost-effectiveness in management of the nodules since doing FNAC in each is expensive while 95% are benign. Kwak et al suggests a modified TIRADS based on number of suspicious ultrasound features and the risk of malignancy. The greater the number of the features the higher the risk of malignancy (26). The Thyroid Imaging Reporting and Data System (TI-RADS) Committee of the American College of Radiology (ACR) published a white paper on a new system for classifying thyroid nodules based on their sonographic features. This system termed ACR TIRADS, gives points in five ultrasound categories namely composition, echogenicity, shape, margin and echogenic foci. Depending on the ultrasound characteristic in a given category, each feature is assigned a point from 0 to 3. The points are then added up to decide the risk level of the nodule from TR1 to TR5. Then final decision like biopsy or follow up is made depending on ACR TIRADS level (27). Moifo B et al published a work on TIRADS based on Russ' modified TIRADS classification. Their study shows the risk of malignancy to be as low as zero percent (0%) in TIRADS 2 category and as high as 100% in TIRADS 5 category (28).

All the above variants have reported excellent concordance between TIRADS criteria and fine needle cytology findings of thyroid nodules. However they are only rarely used in day-to-day practice, possibly due to some complexity, limiting their applicability by the practitioners (24,26,27,29).

The Korean Society of Radiology modified the TIRADS system into K-TIRADS, which is based on greyscale USS characteristics of thyroid nodules. It is relatively easy to apply and particularly centered on the combination of solidity, echogenicity, and suspicious USS features. The suspicious features referred to here are Microcalcification, non-parallel orientation (taller-than-wide) and spiculated/microlobulated margin. A solid hypoechoic nodule with any of the 3 suspicious USS features is considered highly suspicious of malignancy. A solid hypoechoic nodule without the suspicious features or a partially cystic or isoechoic to hyperechoic thyroid nodule with any of the 3 suspicious USS features is considered in the intermediate suspicion category. Partially cystic or isoechoic to hyperechoic nodule without any of 3 suspicious USS features is considered in low suspicion group. A spongiform, cystic or a partly cystic nodule with comet tail artifact is considered benign (23,30). In K-TIRADS thyroid nodules are classified as high suspicion or K-TIRADS 5, intermediate suspicion or K-TIRADS 4, low suspicion or K-TIRADS 3, and benign nodules or K-TIRADS 2. K-TIRADS 1 means no nodule detected on ultrasound (23). The role of size as a predictor of malignancy is debatable (18,23). However, it is stipulated that cancer size has a prognostic value with implications on recurrence and mortality rates. The Korean Society of Radiology recommends FNAC to nodules measuring at least 1cm in TIRADS 4 and 5 categories corresponding to moderate to high malignancy risk. For K-TIRADS 3 nodules FNAC is recommended in cancer lesions measuring at least 1.5cm. If there is tumor extension outside the thyroid, suspected lymph node or distant metastases FNAC is mandatory regardless of nodule size as these suggest poor prognosis (23).

1.2.5 Diagnostic performance characteristics of K-TIRADS and FNAC

With K-TIRADS categories 4 or 5 for nodules ≥ 1 cm and K-TIRADS 3 (for nodules ≥ 1.5 cm) criteria to represent malignancy, the sensitivity and negative predictive values are high but the specificity and accuracy for malignancy are low. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for overall malignancy using this criteria are 94.5%, 26.8%, 27.5%, 94.3%, and 42.2%, respectively. (23,30)

The diagnostic accuracy of FNAC is reported to be high with high positive and negative predictive values and low false positive and false negative rates (6,31).

1.3. Conceptual framework

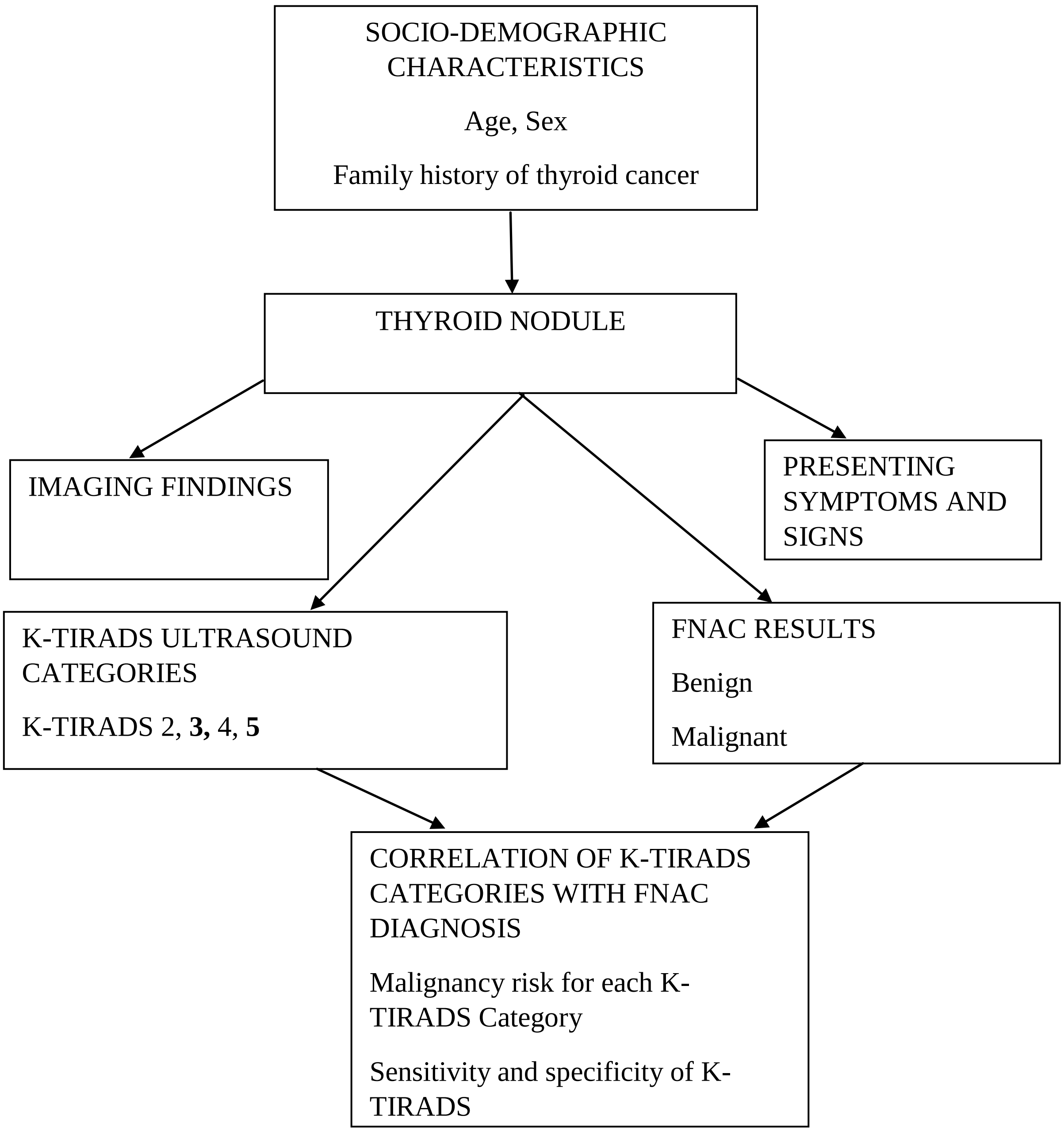


Fig 3: Flow chart showing relationship between independent variables i.e. Age, Sex, family history, history of neck radiation and the dependent variables i.e. USS findings, K-TIRADS USS categories, presenting symptoms and signs of thyroid nodules.

1.4. Problem statement

Thyroid nodules are common worldwide. Their importance is due to the fact that they carry a malignant potential in about 5% of the patients (8).Despite the relatively low prevalence of thyroid malignancy we need to detect the true cases for appropriate management. Family history and history of neck radiation are some of recognized risk factors. Iodine deficiency, is implicated in a large proportion of malignant thyroid nodules in the African setting (17). Ultrasound, Thyroid scintigraphy, CT, PET scan and MRI can be used in the imaging workup of the nodules. However, thyroid Ultrasound is favored as the first investigation modality being cheaper, radiation free and non-invasive. However, there is a wide range of appearance on ultrasound making it challenging to develop a clear diagnosis using this modality. Various studies have been done to characterize the sonographic patterns in the attempt to investigate which features suggest benignity and which are consistent with malignancy. A recently suggested Thyroid reporting and data system by The Korean Society of Radiology (K-TIRADS) has proved useful in sorting features suggestive of malignant nodules as well as those matching with benignity using a combination approach. This system is based on Sonographic greyscale appearance of thyroid nodules irrespective of clinical history. The ultrasound characteristics assessed are solidity or contents of a nodule, shape, echogenicity, margins and presence of microcalcifications. Some other modified risk stratification systems such as ACR TIRADS by the American College of Radiology, TIRADS by Kwak et al and many others have also been suggested with the overall goal to standardize thyroid imaging reporting system and ease communication among practitioners. However most of the suggested classification details are too sophisticated for application in daily practice. Consequently very few institutions have adopted them (26)(27).

By comparison with Fine Needle Aspiration Cytology as the gold standard, this study aims to assess the diagnostic performance of K-TIRADS in the risk stratification of thyroid nodules.

1.5 Rationale

K-TIRADS is applicable to all centers including those with only B mode ultrasound machines available.

Given the shortage of pathology services in the country, K-TIRADS may help in the screening for thyroid malignancy in most centers without pathology services.

K- TIRADS might help to systematize thyroid nodule assessments, ultrasound reports and therefore ease the management process.

K-TIRADS may reduce the need for unnecessary invasive procedures like FNAC or core biopsy in patients with benign thyroid nodules, while suggesting nodules with features of malignancy.

1.6. Research question

Is the Korean thyroid imaging reporting and data system (K-TIRADS) reliable in evaluation of thyroid nodules as diagnosed with FNAC at Muhimbili Tertiary hospitals?

1.7. Objectives

1.7.1 Broad objective

To determine the reliability **of** the Korean Thyroid Imaging Reporting and Data System (K-TIRADS) in evaluation of thyroid nodules in patients referred for thyroid ultrasound at Muhimbili Tertiary hospitals from October 2018 to April 2019.

1.7.2 Specific objectives

- To determine the relationship between socio-demographic factors and nature of thyroid nodule in patients with thyroid nodules referred for thyroid ultrasound.
- To determine ultrasound characteristics of thyroid nodules in patients referred for thyroid ultrasound.
- To determine malignancy risk of each K-TIRADS category in patients with thyroid nodules attending imaging department for thyroid ultrasound.
- To determine the diagnostic performance of K-TIRADS for thyroid nodules (using FNAC as gold standard) in patients attending imaging department for thyroid ultrasound.

CHAPTER TWO

2. MATERIALS AND METHODS

2.1 Type of the study

This was a descriptive hospital based cross sectional study conducted for 6 months from October 2018 to April 2019.

2.2 Study population

Patients referred to Radiology department for thyroid ultrasound at Muhimbili Tertiary Hospitals from October 2018 to March 2019. (Fig **4**)

2.2.1 Inclusion criteria

Patients with thyroid nodules undergoing both thyroid ultrasound and FNAC at Muhimbili Tertiary Hospitals.

Patients who consented to participate in the study.

Thyroid nodules with diameter of 1cm and above.

Patients aged 5 years and above.

2.2.2 Exclusion criteria

Patients with diffuse parenchymal thyroid diseases such as Graves' disease and thyroiditis.

Patients with nodules less than 1cm.

Patients with multiple nodules more than 3, as multiple nodules have been shown to have more potential for benignity (12)

Patients undergoing treatment for thyroid disease.

Patient who decline consent.

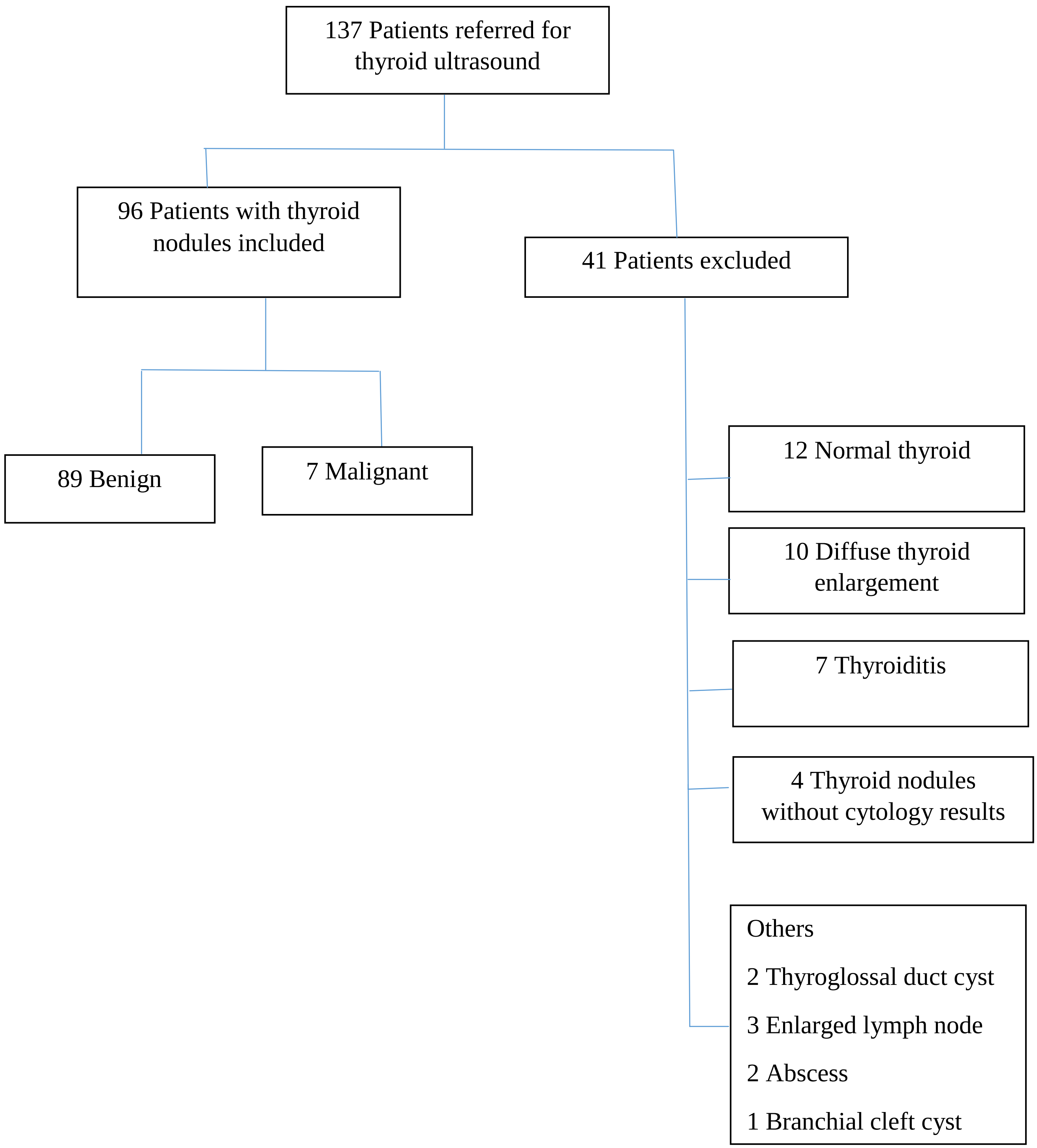


Fig 4. Flow chart of study group

2.3 Sampling and sample calculation

Convenience sampling method was used in which patients with clinical diagnosis of nodular goiter were enrolled in the study consecutively until the required sample size was reached. The sample size was estimated using the fisher's formula;

$$N = \frac{z^2 p\,(100 - p)}{\varepsilon^2}$$

$$= \frac{1.96^2 x 6.7\,(100 - 6.7)}{5^2} = 96$$

Where;

N = Minimum required sample size

z = Percentage point of normal distribution corresponding to 95% level of confidence

ε= Maximum likely error/ margin of error

p= Prevalence of thyroid cancer in Kenya (5).

2.4. Study setting

Ultrasound unit Radiology department Muhimbili National Hospital and MUHAS Academic Medical Centre (MAMC). MNH and MAMC are Public Tertiary Hospitals receiving patients from Dar Es Salaam municipal hospitals and from other Regional and District referral hospitals across the country.

2.5. Data collection

2.5.1 Demographics

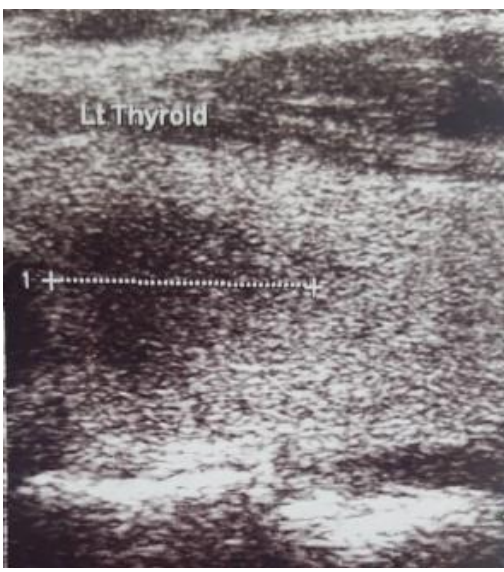
A structured questionnaire was used to collect data. Socio-demographic data of the patients were acquired and recorded in part one of the questionnaire. These included Age, Sex and duration of the disease. Presenting symptoms and signs such as anterior neck swelling, pressure symptoms and presence or absence of pain were enquired.

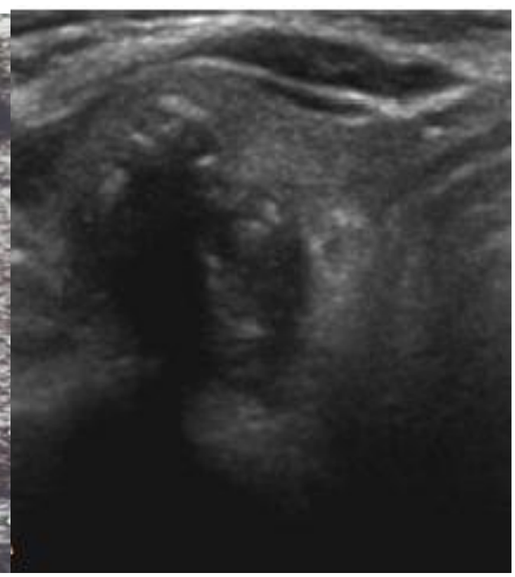
2.5.2 USS Examination and Image Analysis

Thyroid ultrasound was performed using two types of ultrasound machines GE Voluson P8 (USA) and Siemens ACUSON X150™ (Germany) using a linear-array high-frequency probe (5-11 MHz). The neck was scanned in transverse, sagittal and oblique planes while the patient lays in supine position with the head hyperextended. Thyroid ultrasound was performed by the Principal investigator confirmed by a Senior Radiologist. In case of disagreement a second radiologist's opinion was sought and the conclusion was reached by consensus. The nodules were measured in three dimensions i.e. anteroposterior, transverse and sagittal diameter.
Ultrasound findings were recorded in part two of the questionnaire. Ultrasound characteristics were assessed as per the revised Korean Thyroid Imaging Reporting and Data System (K-TIRADS) algorithm (23). These included: solidity/ internal contents, echogenicity, margin, calcification shape and orientation.

Nodules were classified as high suspicion for malignancy (K-TIRADS 5), intermediate suspicion (K-TIRADS 4), low suspicion (K-TIRADS 3) and benign (K-TIRADS 2). According to K-TIRADS there are three suspicious features namely microcalcification, non-parallel orientation (taller-than-wide) and spiculated/microlobulated margin. A solid hypoechoic nodule with any of the 3 suspicious USS features was considered highly suspicious of malignancy (TIRADS 5). A solid hypoechoic nodule without any of the suspicious features fell into intermediate suspicion category (K-TIRADS 4). A partially cystic nodule (having mixed obvious cystic and solid components) with any of the 3 suspicious USS features was considered in K-TIRADS 4 category. Partially cystic nodule without any of 3 suspicious USS features was considered in low suspicion group (K-TIRADS 3). A solid isoechoic or hyperechoic nodule without any suspicious feature was put in K-TIRADS 3 category. Spongiform nodule, purely cystic nodule and partially cystic nodule with comet tail artifacts are considered in the benign category (K-TIRADS 2).

A B





C D

Fig 5. Ultrasound images representing K-TIRADS 2-5

A.K-TIRADS 2-A spongiform nodule (Solid isoechoic with microcystic changes)

B.K-TIRADS 3-A partially cystic nodule without suspicious features.

C. K-TIRADS 4-A solid hypoechoic nodule with ill-defined margin.

D. K-TIRADS 5- A solid hypoechoic taller than wider nodule with microcalcifications

2.5.4 Thyroid FNAC

FNAC was done by pathologist for palpable nodules. For non-palpable nodules the Principal Investigator and pathologist collaborated under USS guidance to take the samples. Inadequate samples had FNAC repeated under ultrasound guidance. Smears for cytology were prepared, interpreted and reported by the Pathologist according to the Bethesda system for reporting thyroid cytology (2).

Final cytological conclusion of the nodule sample was recorded in part 3 of the questionnaire.

Suspicious for malignancy and malignant cytology conclusions were both considered as malignant.

2.6 Data analysis

Statistical Package for Social Sciences (SPSS 23.0 for windows) was be used to analyze data. The mean age of patients was determined. Ultrasound characteristics of each nodule were combined to decide a K-TIRADS category. After determining the K-TIRADS ultrasound categories of thyroid nodule, the risk of malignancy of each TIRADS category was calculated as percentages. The diagnostic performance characteristics of K-TIRADS as a test including Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Values were calculated using FNAC findings as Gold standard.

Frequency distribution bar graphs and two way tables were formulated. Statistical inference was done using X^2 test for categorical variables. Spearman's rank correlation test was used to assess the relationship between categories of K-TIRADS and FNAC results. A p value of less than 0.05 was considered statistically significant at 95% confidence level.

2.7. Ethical considerations

Ethical clearance was sought from MUHAS Research and Publications Committee. Official permission to conduct the study at the Department of Radiology and Imaging of MNH and MAMC was sought. The author adhered to all ethical doctrines as per the Research and Publications Committee standards.

Consent was obtained before proceeding with the study. For children aged less than 18 years, consent was obtained from parents and guardians. Data collection sheets were anonymized.

2.8. Study limitations and mitigation

There might be information and recall bias with the socio-demographic characteristics' records since details such as duration of symptoms or previous history of neck radiation depend on the patient's memory. To solve this, the principal investigator cross checked these issues with the accompanying relatives of the patients.

Conducting the study in tertiary Hospitals may be less representative as the cases are those referred from other hospitals rather than directly from the general community. However, conducting the study in tertiary Hospitals was inevitable as cytopathology services are only available in that level across the country.

With the use of cytology only, as Gold standard in this study, false positive and false negative cytology results may affect the final conclusion without histological validation.

CHAPTER THREE

3. Results

3.1 Socio-demographic characteristics

This study included 96 patients. The age range was from 6 to 92 years. The mean age was 44.5 ±14.7 years.

Table 1. Frequency distribution of age and sex of the study population

Sex	**Frequency**	**Percent**
Male	11	11.5
Female	85	88.5
Total	96	100.0
Age-group(Years)		
≤20	3	3.1
21-40	33	34.4
41-60	49	51.0
61-80	10	10.4
>80	1	1.0
Total	96	100.0

Females were the majority of the study population counting 85 (88.5%). The male to female ratio was 1.8.

Majority of the study subjects were in the age group 41-60 years constituting 51% of the study population followed by 21-40 group which constituted 34.4%.(Table1)

3.2 Relationship between socio-demographic factors and nature of thyroid nodule

Table 2. Relationship between age group and nature of thyroid nodule

Age-group(Years)	Cytology results		Total	P-Value(X^2 test)
	Benign (%)	Malignant (%)		
≤20	3(100)	0(0)	3	
21-40	33(100)	0(0)	33	
41-60	45(91.8)	4(8.2)	49	0.001
61-80	8(80)	2(20)	10	
>80	0(0)	1(100)	1	
Total	89	7	96	

Key: Numbers in parentheses are percentages.

Seven 7(7.3%) cases out of 96 were malignant while the rest were benign. The proportion of malignant nodules in individuals aged 40 and below was zero (n=36) while all malignant cases were found in above 40years age groups.(Table 2) The observed association between age and cytology results was statistically significant (*P<0.01*).

Table 3. Relationship between sex and the nature of thyroid nodule.

Sex	Cytology results		Total	P-Value(X^2 test)
	Benign (%)	Malignant (%)		
Male	10(90.9)	1(9.1)	11	
Female	79(92.9)	6(7.1)	85	0.59
Total	89	7	96	

Key: Numbers in parentheses are percentages.

There was no significant difference in proportion of males with thyroid malignancy compared to that of females .(*p>0.05*). (Table 3)

3.3 Ultrasound characteristics of thyroid nodules

Table 4. Different Ultrasound features of thyroid nodules and their malignancy risks.

USS Characteristics		Cytology results		Total	P value
		Malignant(%)	Benign(%)		
Size					
Maximum diameter	≥1.5cm	7(8.1)	79(91.9)	86	
	<1.5cm	0(0)	10(100)	10	0.45
	Total	7	89	96	
Orientation					
Non parallel	Yes	1(33.3)	2(66.7)	3	
	No	6(6.5)	87(93.5)	93	0.2
	Total	7	89	96	
Shape					
Irregular	Yes	2(66.7)	1(33.3)	3	
	No	5(5.4)	88(94.6)	93	0.01
	Total	7	89	96	
Internal contents					
Solid	Yes	4(9.5)	38(90.5)	42	
	No	3(5.6)	51(94.4)	54	0.7
	Total	7	89	96	
Cystic	Yes	0(0)	10(100)	10	
	No	7(8.1)	79(91.9)	86	0.45
	Total	7	89	96	
Predominantly solid	Yes	3(15.8)	16(84.2)	19	
	No	4(5.2)	73(94.8)	77	0.14
	Total	7	89	96	
Predominantly cystic	Yes	0(0)	2(100)	2	
	No	7(7.4)	87(92.6)	94	0.86
	Total	7	89	96	
Spongiform	Yes	0(0)	22(100)	22	
	No	7(9.5)	67(90.5)	74	
	Total	7	89	96	0.15
Echogenicity					
Hypoechoic	Yes	3(42.9)	4(57.1)	7	
	No	4(4.5)	85(95.5)	89	
	Total	7	89	96	0.008
Isoechoic	Yes	3(4.9)	58(95.1)	61	
	No	4(11.4)	31(88.6)	35	
	Total	7	89	96	0.2
Hyperechoic	Yes	1(5.9)	16(94.1)	17	0.64

	No	6(7.6)	73(92.4)	79	
	Total	7	89	96	
Margin					
Ill defined	Yes	5(17.9)	23(82.1)	28	
	No	2(2.9)	66(97.1)	68	
	Total	7	89	96	0.02
Spiculated	Yes	1(100)	0(0)	1	
	No	6(6.3)	89(93.7)	95	
	Total	7	89	96	0.07
Smooth	Yes	1(1.5)	66(98.5)	67	
	No	6(20.7)	23(79.3)	29	
	Total	7	89	96	0.003
Calcification					
Microcalcificaton	Yes	1(100)	0(0)	1	
	No	6(6.3)	89(93.7)	95	
	Total	7	89	96	0.07
Macrocalcification	Yes	1(50)	1(50)	2	
	No	6(6.4)	88(93.6)	94	
	Total	7	89	96	0.14

Spiculated margins and microcalcification were found to have the highest risk of thyroid malignancy (100%), followed by ill-defined margins (17.9%). However the observed values were not statistically significant (*p=0.07*)

The malignancy risk of the hypoechoic nodules was higher (42.9%) than that of the isoechoic (4.9%) or hyperechoic nodules (5.9%). This difference was statistically significant particularly in favour of hypoechogenicity as an independent predictor of malignancy. (*P<0.01*)

The predominantly solid feature showed a risk of 15.8%. Nodules that measured ≥1.5cm maximum diameter demonstrated a higher risk of malignancy compared to nodules measuring <1.5cm. However this difference between them was not statistically significant (*p>0.05*).

Irregular shape had higher risk of malignancy (66.7%) (*p<0.05*) than round to oval shape (5.4%)

Non-parallel (Taller than wide) orientation demonstrated increased risk of malignancy (33.3%) relative to parallel orientation (6.5%). However the difference in the risk was not statistically significant. (*p>0.05*)

Cystic, predominantly cystic and spongiform appearance features demonstrated zero risk of malignancy. (Table 4)

Table 5.Summary of the diagnostic performance of the major USS features.

USS Characteristics		Cytology results Malignant (%)	Benign(%)	Total	P -value
Hypoechogenicity	Yes	3(**42.9**)	4	7	
	No	4	85(**95.5**)	89	
	Total	7	89	96	0.008
Non parallel orientation	Yes	1(**14.3**)	2	3	
	No	6	87 (**97.8**)	93	
	Total	7	89	96	0.2
Spiculated margin	Yes	1(**14.3**)	0	1	
	No	6	89(**100**)	95	
	Total	7	89	96	0.07
Microcalcification	Yes	1(**14.3**)	0	1	
	No	6	89 (**100**)	95	
	Total	7	89	96	0.07

Key: Numbers in parentheses are column percentages.

The USS The "major" USS features that are reported to be highly predictive of malignancy include hypoechogenicity, non-parallel orientation, spiculated/microlobulated margins, and presence of microcalcification. (32) These were analyzed in comparison to cytology. Their sensitivity, specificity, predictive values were calculated. The sensitivity and specificity for hypoechogenicity were 42.9% and 95.9% respectively with a p-value of 0.008. Non–parallel orientation, spiculated margin and microcalcification had specificities of 97.8%, 100% and 100% respectively. They showed similar sensitivities (14.3%) with p-values > 0.05 (Table 5)

3.4 K-TIRADS ultrasound categories of thyroid nodules

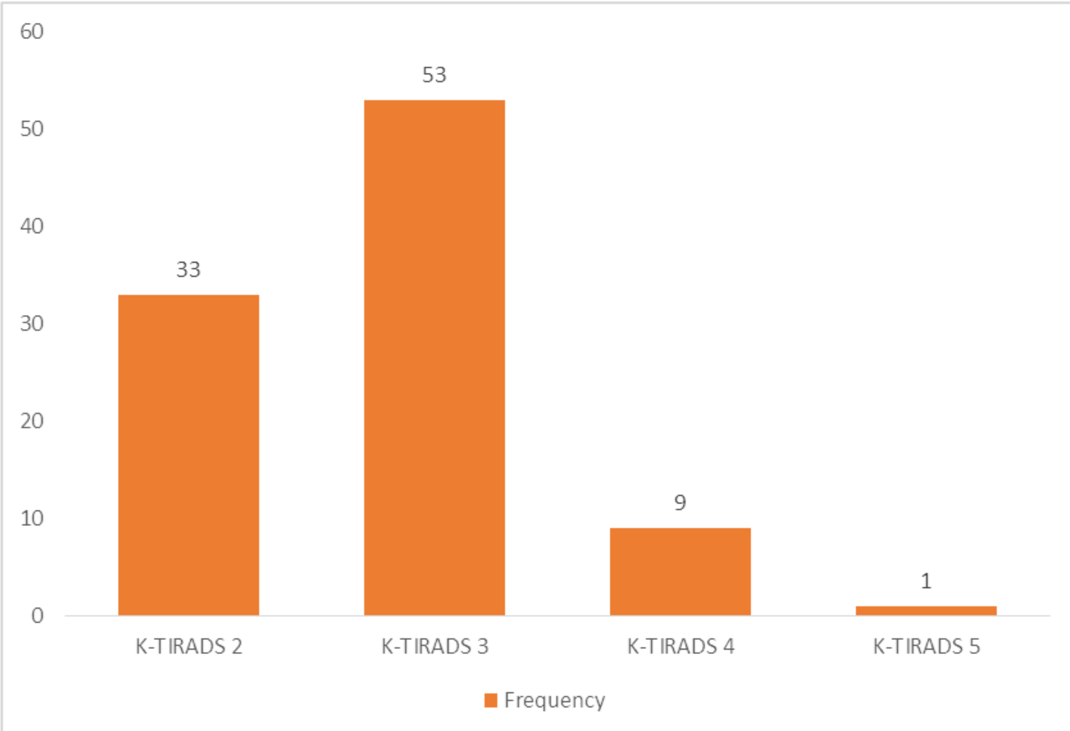


Fig 6. Bar chart showing frequency distribution of K-TIRADS USS categories of the study population (n=96)

Number of patients in K-TIRADS 3 category was the highest 53(55.2%) followed by K-TIRADS 2 which had 33(34.4%) then K-TIRADS 4 with 9(9.4%) and the least was K-TIRADS 5 with 1 (1%).This shows that K-TIRADS 3 nodules were the most prevalent of all other categories. (Fig 6)

3.5 Malignancy risk of each K-TIRADS category.

Table 6. K-TIRADS categories and their malignancy risks

K-TIRADS Category	Cytology results		Total	Malignancy risk	Spearman's rho	
	Malignant	Benign		(%)	Coefficient	P-Value
K-TIRADS 2	0	33	33	0		
K-TIRADS 3	2	51	53	3.8		
K-TIRADS 4	4	5	9	44.4	0.39	0.000
K-TIRADS 5	1	0	1	100		
Total	7	89	96	–		

The risk of malignancy was 0% in K-TIRADS 2 category, 3.8% in K-TIRADS 3, 44.1% in K-TIRADS 4 and 100% in K-TIRADS 5 category. The trend shows increase of risk of malignancy with the order of K-TIRADS, the lowest risk being in K-TIRADS 2 with intermediate risk in K-TIRADS 4 and the highest in K-TIRADS 5 (Table 6).

3.6 Diagnostic performance of K-TIRADS for thyroid nodules (FNAC as gold standard)

Table 7. Diagnostic performance of K-TIRADS

Status by K-TIRADS Category	Cytology results		Total	
	Malignant (%)	Benign(%)		P-Value
MALIGNANT	7 (**100**)	51	58	<0.01
BENIGN	0	38 (**42.7**)	38	
Total	7	89	96	

Key: Numbers in parentheses are column percentages.

Considering K-TIRADS 3 (with nodules ≥1.5cm), K-TIRADS 4 and K-TIRADS 5 as criteria for malignancy the sensitivity, specificity, positive predictive, and negative predictive values were respectively 100%, 42.7%, 12.1% and 100%. ($p<0.05$) (Table 7).

CHAPTER FOUR

4. Discussion

This was a cross sectional hospital based study conducted to assess reliability of K-TIRADS, recommended by the Korean Society of Radiology for thyroid nodules workup. The ultrasound findings were compared with FNAC results as a gold standard test for deciding the nature of thyroid nodule(s).

Nodular goiter is largely the disease of females with Male: Female ratio of 1:7-13 (12). Our study supports the same finding with similar Male to female ratio of 1:8. The reason for females being more affected is probably due to the role of hormonal influence which is different in females from males.

In this study all cases of malignant nodules were found in people aged above 40 years. There was no positive case for malignancy in the below 40 age group. Dean et al. (7) reports a higher thyroid malignancy rate in patients aged above 40 .This study reveals similar findings. As with other types of malignancies the reason for the higher rate of malignancy in the old population in our cases could be due to decreased body immunity with aging. Another possibility could be the fact that thyroid nodule individuals above 40 years have had a prolonged time to live with the condition which gives time for malignant transformation of the thyroid nodules.

Despite the fact that thyroid nodules are far more prevalent in females compared to male subjects this study reveals no significant difference in proportions of thyroid cancer between males and females ($p>0.05$). This is contrary to a study by Gharib et al. (18) which reports increased risk of thyroid malignancy in males relative to females.

Cystic nodules, predominantly cystic and spongiform appearance had zero risk of malignancy in this study. This finding is supported by other previous studies. (23,30)

The risk of malignancy is higher (20.6-70.4%) in hypoechoic thyroid nodules compared to isoechoic, and hyperechoic nodules. (19,26,30,32) .This study showed similar results with a risk of 42.9% (*P<0.01*) in favor of hypoechogenicity hence supporting the findings by other authors.

Spiculated margins and microcalcification showed the highest specificity for malignancy (100%) in this study though the observed values were not statistically significant (*P=0.07*). However despite the higher specificities the sensitivities are lower. This supports the opinion that individual ultrasound characteristics are inadequate in risk stratification of thyroid nodules.

Studies reveal that non parallel orientation has less sensitivity but very high specificity for thyroid malignancy (88.4-100%) and positive predictive value of 71.2-100%. (23,26,28,30) Our findings were in agreement with these outcomes. This further demonstrates decreased diagnostic performance of ultrasound characteristics when used individually.

Regarding the diagnostic value of the highly suspicious USS features namely microcalcifications, spiculated or microlobulated margins and taller than wide orientation, this study demonstrated their high specificities and Negative Predictive Values for diagnosing thyroid cancer. However, their positive predictive values for cancer are partly diminished by their low sensitivities such that no single USS characteristic by itself can reliably predict malignancy.

The combination of hypoechogenicity of the nodule with at least one or more USS features suggestive of malignancy commendably raises the performance of USS in predicting the risk of malignancy. (18,20–24,26) This study reveals consistent results with high specificities and low sensitivities of hypoechogenicity, further supporting the opinion that using hypoechogenicity alone is not sufficient in predicting malignancy using ultrasound.

Large proportion of study subjects were in K-TIRADS category 3(55.2%) followed by K-TIRADS 2(34.4%). In a study by Moifo et al. (28) K-TIRADS 3 was reported to be the dominant category with percentage similar to the one was found in this study. This finding reflects the high prevalence of benign nodules and low prevalence of malignant thyroid nodules since K-TIRADS 3 and K-TIRADS 2 are in the low suspicion and benign categories respectively and do not include any of the suspicious features namely non-parallel orientation, microalcification and speculated/microlobulated margins.

The risk of malignancy was found to increase from K-TIRADS 2 through K-TIRADS 5. K-TIRADS 2 had 0% malignancy risk while K-TIRADS 5 had the highest (100%) risk. This finding is in agreement with the Korean Society of Radiology Consensus Statement and Recommendations by Shin JH et al (23) which reported malignancy risk of K-TIRADS 2, K-TIRADS 3, K-TIRADS 4 and K-TIRADS 5 to be <1%,3-5%, 15-50% and >60% respectively. Using Russ' modified TIRADS classification Moifo et al (28) reported a substantial increase in malignancy risk from TIRADS 3 to 5. This study revealed similar findings. Thyroid cancers were found in the TIRADS 3, 4 and 5 categories.

We can infer from the results of this study that most malignant nodules have USS features that may fall in low suspicion category, intermediate or high suspicion categories. So for the malignant nodules very few can be put in one category of typical ultrasound features that are consistent with malignancy. This substantiates the value of incorporating cut off size and advocacy for FNAC when nodules are not typically benign on USS using K-TIRADS criteria.

In this study, combining K-TIRADS 3 (for nodules ≥ 1.5 cm), K-TIRADS 4 and 5 to represent malignancy, both the sensitivity and NPV values were very high (both 100%). The specificity, PPV and accuracy of USS for malignancy were low. These findings were statistically significant (p<0.01). The reason for low predictive values is most likely due to relatively lower prevalence of malignant thyroid nodules. These findings are consistent with Na D.G et al and Shin JH et al reports.(23,30). This implies that in order to detect all malignant cases by USS we need to regard the low suspicion nodules with size equal to or above 1.5cm, intermediate suspicion and high suspicion K-TIRADS categories as malignant. However, this will count a proportion of benign nodules as malignant since this criterion demonstrates low specificity (42.7%). Therefore, we need to subject the malignant cases obtained with this criteria to a second test to remove the false positives. This implies that we still need to go for FNAC when thyroid nodules do not have typical benign features using K-TIRADS algorithm. This notion is in keeping with the recommendations by the Korean Society of Radiology (23).

CHAPTER FIVE

5. Conclusion and Recommendations

5.1 Conclusion:

Females constitute the majority of thyroid nodule patients.

Age above 40 years is a risk for thyroid malignancy.

Majority of thyroid nodules are in K-TIRADS 3 category.

Malignancy risk increases with the order of K-TIRADS category.

K-TIRADS criteria demonstrates a very high sensitivity for thyroid malignancy and therefore a reliable screening tool.

5.2 Recommendations

Patients with thyroid nodules can undergo ultrasound assessment using K-TIRADS as the first modality.

Patients diagnosed with benign thyroid nodules using K-TIRADS may not need further invasive screening (e.g FNAC).

A community based study with a large sample is suggested to obtain more evidence for implementation of K-TIRADS.

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Appendix I : K-TIRADS Algorithm

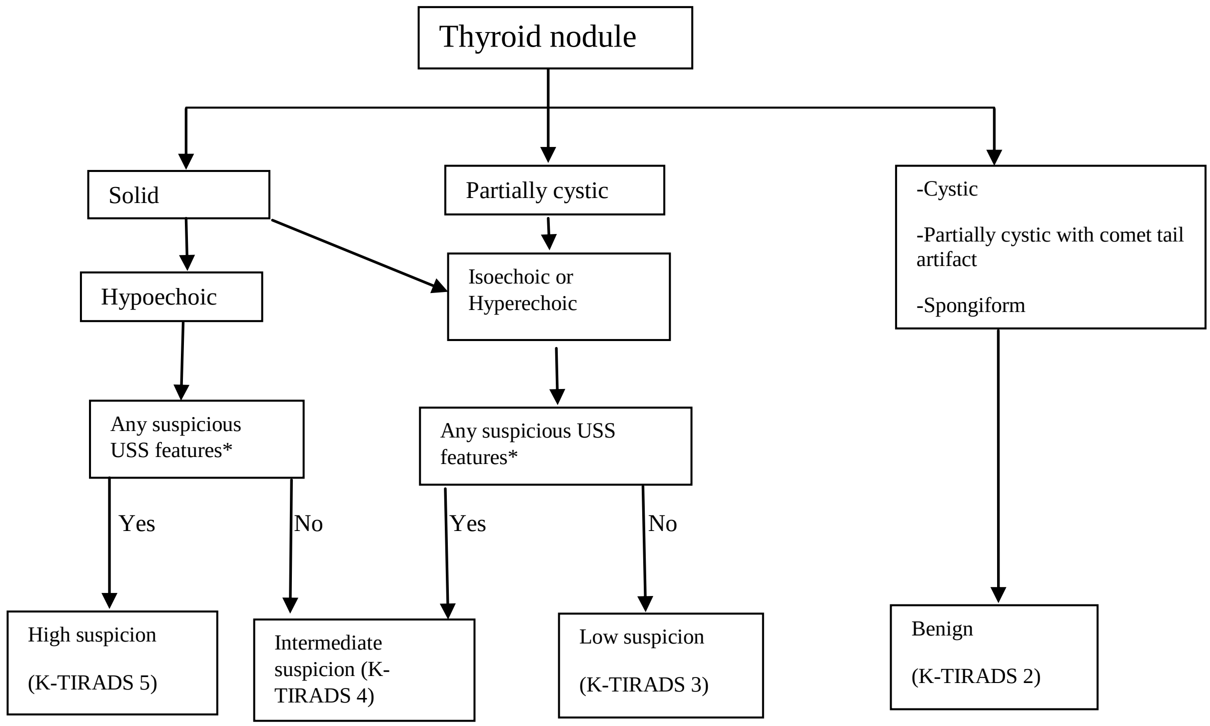

Fig 4. K-TIRADS Classification algorithm for malignancy risk stratification.(23)

*Microcalcification, nonparallel orientation, spiculated/microlobulated margin. USS = ultrasonography.

Appendix II: Questionnaire

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

SCHOOL OF MEDICINE - DEPARTMENT OF RADIOLOGY

ID No ………… Date……

Part 1 Demographics

I.Age **………** **Sex 1.M 2.F**

II.Presenting symptom & signs

Anterior neck swelling	1. Yes	2. No
Pain	1. Yes	2. No
Pressure symptoms (Dyspnea)	1. Yes	2. No
Duration	.... (Months)	

III. Risk factors

Positive family history	1.Yes	2. No
History of neck radiation	1.Yes	2. No

Part 2. Thyroid nodule Imaging findings

I. Nodule size

Anteroposterior(AP) diameter………….cm

Transverse(TR) diameter……...cm. Longitudinal(Long) diameter……….cm

AP/TR Diameter……. AP/Long Diameter…….cm

Maximum diameter ....cm Volume of nodule........cc

Orientation 1. Parallel 2. Non parallel (Taller than wide)

Shape 1. Round/oval 2.Irregular (Regardless of orientation)

II.Internal content

1. Solid (No obvious cystic portion)

2.Cystic (No solid portion) (Go to No IV)

For mixed nodules: Volume of solid component……cc. Volume of cystic component…...cc. (Calculated from volume=lengthxwidthxheightx0.52)

3. Predominantly solid (Cystic portion less or equal to half the nodule size)

4. Predominantly cystic (Cystic portion more than half of the nodule size)

5. Spongiform appearance (Isoechoic nodule with microcystic change involving half or more of the nodule)

6. Partially cystic nodule with comet tail artifacts

III. Echogenicity 1. Hypoechoic 2. Isoechoic 3. Hyperechoic (For lesions with solid component)

IV. Margin 1. Smooth 2. Ill-defined/Indistinct 3. Spiculated/Microlobulated

V. Calcification (For solid and partially cystic nodule) 1.Yes 2. No

VI. Type of Calcification 1.Microcalcification 2. Macrocalcification

VII. K-TIRADS Ultrasound Classification

1. K-TIRADS Category 2
2. K-TIRADS Category 3
3. K-TIRADS Category 4
4. K-TIRADS Category 5

Part 3: <u>Cytology results</u>

1. Benign
2. Malignant

Appendix III: Consent Form (English Version)

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

DIRECTORATE OF RESEARCH AND PUBLICATIONS, MUHAS

Consent to Participate in a Study

ID-NO……

My name is Dr. Seleman Fadhili. I am conducting a study on "Assessment of the role of TIRADS in evaluation of thyroid nodule, in comparison with Bethesda Fine Needle Aspiration Cytology in patients attending Muhimbili hospitals from July 2018 to January 2019"

The purpose of the study is to see how we can improve the imaging and reporting of thyroid nodules using ultrasound. The outcome of the research will aid in the improvement of quality of this modality of investigation and thus final management.

How to be involved

Patients who agree to participate in this study you will be required to sign the consent form, give details of their socio-demographic data and finally undergo ultrasound examination. This will not cause any pain. After ultrasound scanning the experts including the researcher will plan and take a sample from the lesion using a needle. This will be painful. We will use medicine to prevent pain on the site of needle injection. The sample will then be interpreted in the laboratory for your results.

Confidentiality

The information obtained from you will be confidential. No name will appear on any document of this study instead Identification numbers will be used. The remnants of your sample will be discarded safely after laboratory interpretation.

Participation and Right to Withdraw

Involvement in this study is voluntary. You can participate or refuse to participate from this study. Refusal to participate from this study will not affect your management.

Benefits

The study outcomes will help to improve imaging and reporting of thyroid nodules, consequently management of patients with this condition.

Contacts

If you ever have questions about this study, you should contact the Principal Investigator, Dr. Seleman Fadhili, Muhimbili University of Health and Allied Sciences, P. O. Box 65001, Dar es Salaam. Tel. 0717015632**.**

In case you have questions about your rights of participation in this study, you may contact **Dr. Bruno Sunguya, Chairperson of the Senate Research and Publications Committee**, P. O. Box 65001 DSM. Telephone**:** **+**255 022 2152489 or Prof. Ahmed Jusabani who is the supervisor of this study (Tel. +255 713 273 890)

Participant agrees

I ………………………………………. have read the contents in this form. My questions have been answered. I am willing to participate in this study.

Signature of participant …………………………Date…….………

Signature of Researcher ………………………..Date…………….

Appendix IV: Consent Form (Swahili Version)

CHUO KIKUU CHA AFYA NA SAYANSI SHIRIKISHI MUHIMBILI

KURUGENZI YA TAFITI NA UCHAPISHAJI

Ridhaa ya kushiriki kwenye utafiti

Namba ya utambulisho ---

Habari! Jina langu ni Dkt Seleman Fadhili. Ninafanya utafiti wenye lengo la kutathmini nafasi ya Mfumo wa kuripoti kipimo cha utrasaund ya tezi shingo uitwao TIRADS ikioanishwa na majibu ya kipimo cha sampuli inayochukuliwa kwa sindano kwenye tezi la shingo katika Hopitali ya Taifa Muhimbili..

Dhumuni la Utafiti huu ni kuona namna ya kuongeza ufanisi wa mfumo huo hivyo kurahisisha utoaji wa ripoti za ultrasound ya tezi la shingo. Matokeo ya utafiti huu yatasaidia katika kuinua ubora wa kipimo hiki. Jinsi ya kushiriki

Ukikubali kushiriki katika utafiti huu, utasailiwa halafu utaendelea na kipimo cha ultrasaund. Kipimo hiki hakisababishi maumivu yoyote. Baada ya hapo wataalamu akiwemo mtafiti mkuu watapanga na kuchukua kipimo kutoka kwenye uvimbe kwa kutumia sindano. Hiki kitakuwa na maumivu. Hata hivyo tutaweka dawa ya ganzi ili kuzuia maumivu wakati wa kuchukua kipimo. Baada ya hapo sampuli itapelekwa maabara kwa ajili ya majibu ya kipimo.

Usiri

Taarifa zote zitakazokusanywa kupitia dodoso hili zitakuwa ni siri. Jina lako halitatumika

badala yake tutatumia namba ya utambulisho. Baada ya kusomwa mabaki ya sampuli yako yatatupwa sehemu salama na hayatatumika kwa madhumuni yoyote ya ziada.

Uhuru wa kushiriki na haki ya kujitoa

Kushiriki kwenye utafiti huu ni hiari. Unaweza kushiriki au kukataa kushiriki na hii haitakuondolea haki ya kupata matibabu .

Faida

Matokeo ya utafiti huu yatasaidia kuinua mfumo wa ufanyaji na utoaji wa taarifa za ultrasound ya tezi la shingo hivyo kuinua kiwango cha huduma kwa wagonjwa.wa aina hii.

Mawasiliano

Ikiwa una maswali zaidi juu ya utafiti huu, usisite kuwasiliana na mtafiti, Dr. Seleman Fadhili, wa Chuo Kikuu cha afya na sayansi shirikishi Muhimbili, S. L. P 65001, Dar es Salaam. Simu; 0717015632.

Ikiwa una maswali juu ya haki yako ya kushiriki katika utafiti huu, unaweza kuwasiliana na **Dkt Bruno Sunguya, Mwenyekiti wa Kamati ya Utafiti na uchapishaji, S. L. P 65001 DSM. Simu: +255 022 2152489 au Prof Ahmed Jusabani ambaye ni msimamizi wa utafiti huu. (Simu+255 713 273 890)**

Nakubali

Mimi.....................................nimesoma na kuelewa maelezo ya fomu hii. Maswali yangu yamejibiwa na nipo tayari kushiriki.

Sahihi ya mshiriki ……………………… Tarehe…….………

Sahihi ya mtafiti ………………………......Tarehe…………….

Appendix V: Ethical Clearance

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

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Ref. No. DA.287/298/01A/

25th September, 2018

Dr. Seleman Fadhili
MMed. Radiology
MUHAS.

RE: APPROVAL OF ETHICAL CLEARANCE FOR A STUDY TITLED: "THE RELIABILITY OF K-TIRADS IN EVALUATION OF THYROID NODULES, CORRELATION WITH BETHESDA FNAC IN MUHIMBILI TERTIARY HOSPITALS, 2018"

Reference is made to the above heading.

I am pleased to inform you that, the Chairman has, on behalf of the Senate, approved ethical clearance for the above-mentioned study. Hence you may proceed with the planned study.

The ethical clearance is valid for one year only, from 24th September, 2018 to 23rd September, 2019. In case you do not complete data analysis and dissertation report writing by 23rd September, 2019, you will have to apply for renewal of ethical clearance prior to the expiry date.

Dr. Emmanuel Balandya
ACTING: DIRECTOR OF POSTGRADUATE STUDIES

cc: Director of Research and Publications
cc: Dean, School of Medicine, MUHAS